Working memory in very-low-birthweight children at the age of 11 years

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Abstract

The aim of this study was to investigate the working memory (WM) of very-low-birth-weight (VLBW, ≤ 1500 g) children at the age of 11 years using Baddeley's WM model. The regional cohort of 95 VLBW children was assessed for the domains of the WM model (central executive [CE], visuospatial sketchpad [VS], and phonological loop [PL]) using subtests from the Working Memory Test Battery for Children and the WISC-IV. VLBW children were categorized into three groups according to their degrees of brain pathology (normal, minor, or major) in neonatal brain magnetic resonance imaging at the term age, and the WM performance was compared between groups to test norms. The structure of the WM model was studied by analyzing correlations among domains. Even VLBW children with normal cognitive development (general ability index ≥ 85) performed poorer compared to the test norms (M = 100, SD = 15) in CE (M = 87.64, SD = 20.54, p < .001) and in VS (M = 91.65, SD = 11.03, p < .001), but their performance in PL was above the norm (M = 110.79, SD = 13.79, p < .001). VLBW children with major brain pathology performed significantly poorer compared to other groups in VS and PL. The correlations among the WM domains of the VLBW children differed from earlier findings in normative populations. To conclude, the WM of VLBW children differed especially in CE and VS from the normative population irrespective of the degree of brain pathology or the level of cognitive development.

Keywords: working memory, preterm, phonological loop, central executive, visuospatial sketchpad, brain pathology, magnetic resonance imaging

Working Memory in Very-Low-Birth-Weight Children at the Age of 11 Years

In recent decades, the care of very preterm (< 32 gestational weeks) and very-low-birth-weight (VLBW, < 1501 g) children has developed significantly (Allen, Cristofalo, & Kim, 2011; Johnson, Wolke, Hennessy, & Marlow, 2011; Milligan, 2010). Despite improving survival rates (Horbar et al., 2012), the cognitive development of very preterm infants lags behind that of their peers (Allen et al., 2011; Johnson et al., 2011; Milligan, 2010). Moreover, preterm children often have learning difficulties at school and need additional support (Larroque et al., 2011; Pritchard, Bora, Austin, Levin, & Woodward, 2014).

It has been shown that one's capacity for working memory (WM) plays a central role in academic achievements. Alloway and Alloway (2010) described the concept of a so-called bottleneck phenomenon while referring to a narrow WM leading to poorer academic performance (Mulder, Pitchford, & Marlow, 2010; Simms et al., 2015). WM has been described as a system that distributes and stores received information during cognitive processes via three domains (Baddeley, 1996; Baddeley & Hitch, 1974). The central executive (CE) monitors two subsystems, the visuospatial sketchpad (VS) and the phonological loop (PL), and it directs attention toward the ongoing task (Baddeley, 1996). The CE also connects these subsystems to long-term memory (Baddeley, 1996). The VS stores, for example, the location of a figure or the figure itself, and the PL handles and stores phonetic information (Baddeley, 1986).

Gathercole, Pickering, Ambridge, and Wearing (2004) applied Baddeley's original WM model to children and found that this three-domain system is distinguishable in children from 6 years of age onward. The CE is strongly connected to the PL and the VS, while these two subsystems are relatively independent of each other. In a more recent study, Michalczyk, Malstädt, Worgt, Könen, and Hasselhorn (2013) demonstrated the same structural phenomenon in 5-to-12-year-old children. Van der Molen (2010), on the other hand, showed a different WM structure with children and adolescents who had minor to major cognitive impairments. She found a separate PL component and a more general memory component with correlational loadings on the CE and the VS.

Studies on VLBW children have shown that deficits in WM functioning are common (e.g., Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlan, 2009; Rose, Feldman, Jankowski, & van Rossem, 2011). Recent studies have shown that WM deficits in preterm-born children may appear despite having normal cognitive capacity and being without major disabilities (Aarnoudse-Moens et al., 2012; Farooqi, Adamsson, Serenius, & Hägglöf, 2016; Luu, Ment, Allan, Schneider, & Vohr, 2011; Wehrle et al., 2016). Visuospatial WM functions especially have been found to be vulnerable in preterm children (de Kieviet, van Elburg, & Oosterlaan, 2012; Jongbloed-Pereboom, Janssen, Steenbergen, & Nijhuis-van der Sanden, 2012). The field involving verbal memory research on preterm-born children has been heterogeneous, and the results have been confusing as to whether clear deficits exist (e.g., Dall'Oglio et al., 2010; Luu et al., 2011) or not (e.g., Fraello et al., 2011; Lind et al., 2011).

According to earlier studies, VLBW children with major brain pathology are at an increased risk for poor cognitive development (e.g., Kidokoro et al., 2014; Lind et al., 2010; Munck et al., 2010; Northam, Liégeois, Chong, Wyatt, & Baldeweg, 2011; Radic, Vincer, & McNeely, 2015). In addition, early severe brain injuries affect the WM functions of preterm-born children (Omizzolo et al., 2014; Woodward, Edgin, Thompson, & Inder, 2005; Zubiaurre-Elorza et al., 2012). Clark and Woodward (2010) demonstrated that even mild brain abnormalities can be associated with visuospatial WM deficits, and more severe injuries can also cause problems in verbal WM. Aside from this, even without an evident brain injury detected by conventional magnetic resonance imaging (MRI), the maturation of the brain has shown to change after preterm birth, and this alteration results in less mature and atypically formed brain networks (Smyser et al., 2010). Of these networks, hippocampal-cortical ones especially have been stated to be responsible for deficits in the CE domain (for a review, see Nosarti & Froudist-Walsh, 2016).

The WM performance of VLBW children has previously been studied, mostly with separate memory tasks focusing on specific memory functions (e.g., Aarnoudse-Moens et al., 2012; Clark & Woodward, 2010; de Kieviet et al., 2011; Jongbloed-Pereboom et al., 2012). According to meta-analyses by Jongbloed-Pereboom et al. (2012), and recently by Nosarti and Froudist-Walsh (2016), the challenge of comparing different WM studies is evident due to different definitions of prematurity, diversity of methods applied, and wide age range of VLBW children at the assessment point. The WM structure of VLBW children has not been observed previously according to a comprehensive theoretical framework. Therefore, the objective of this study was to investigate WM in VLBW children using Baddeley’s WM model applied to children (Gathercole et al., 2004). The aims were (a) to study the WM performance of the VLBW group and compare it to the test norms, (b) to study the effects of the cognitive level (general ability index [GAI]) and the degree of brain pathology, and (c) to study the correlation structure among the three WM domains. The hypothesis in this study was that VLBW children would have below-average performances in the WM model’s domains, especially in VS, compared to the test norms. It was also hypothesized that in the VLBW group, low overall cognitive levels and more severe degrees of brain pathology would be associated with lower WM performance. Lastly, it was hypothesized that the WM correlational structure of the VLBW children would correspond to Gathercole’s modification of Baddeley’s model.

Methods

Participants

This study was a part of a multidisciplinary follow-up study, PIPARI (Development and Functioning of Very Low Birth Weight Infants from Infancy to School Age). All VLBW (≤ 1500 g) infants born preterm at Turku University Hospital (Finland) between January 2001 and April 2004 were included. The Ethical Committee of the Hospital District of Southwest Finland approved the study protocol. All parents and children who agreed to participate in this study gave written informed consent after written and oral information was provided.

A total of 151 VLBW children were born during the data collection period; of these, 23 (15%) died. One child was excluded due to a genetic syndrome, two were born in another hospital, and three were living outside of the catchment area. Only Finnish-speaking children with at least one Finnish-speaking parent were included. Those children who could not be assessed in Finnish (e.g., children using sign language) or assessed at all (e.g., due to severe cognitive impairment) were also excluded. A total of seven children did not fulfill the language criteria. Twenty out of 115 eligible children withdrew or refused to participate. The final study population consisted of 95 VLBW children. One child out of the 95 (1%) used a hearing aid, and eight children (8%) had cerebral palsy. The 20 children who withdrew or refused to participate were compared to the final study population according to the demographic characteristics shown in Table 1. A significant difference was found only in two characteristics; in the group of 20 children, there were significantly fewer multiple births (p = .03) and a significantly lower maternal education level (p = .001).

An additional data sample was collected to study whether or not the original British test design translated into the Finnish language from the Working Memory Test Battery for Children (WMTB-C) could be applied in a Finnish population (Pickering & Gathercole, 2001). Data were collected from three schools in the capital area of Finland. A research psychologist (S. K.) recruited the children by contacting school psychologists and the headmasters of schools in socioeconomically representative areas. The teachers of five mainstream fifth-grade classes from three schools were invited, and all agreed to participate. Seventy-eight non-selected pupils

(63%) and their parents agreed to participate and gave written consent after written information was provided. Ten out of these 78 participants were not included in the statistical analysis (eight children did not speak Finnish as their mother tongue, one was born a year earlier, and one family did not return the required background-information form). The final group consisted of 68 children. The research psychologist collected the data at the school during school days.

Demographic Characteristics

The demographic and neonatal characteristics of the VLBW children were collected in the neonatal intensive care unit (see Table 1).

(Table 1 about here)

The background variables of the 68 children who formed the sample group for the WMTB-C subtests were collected from their parents via questionnaires before testing. In the sample group, 23 children were males (34%), the mean birth weight was 3492.76 g (*SD* = 616 g, range 1000–4705 g), and the mean gestational age in weeks was 39.57 (*SD* = 1.85, range 30–42, data missing for three children). Maternal education was nine years or less for 10% of the children, more than nine to 12 years for 46%, and more than 12 years for 44%. Paternal education (data missing for four children) was nine years or less for 6% of the children, more than nine to 12 years for 54%, and more than 12 years for 39%.

Assessing the Cognitive Development and Working Memory (WM) of VLBW Children

A neuropsychologist (A. N.) collected the data concerning the cognitive development and WM of the VLBW children during the autumn term of the year when the children turned 11 years. All of the assessments were conducted during one session at Turku University Hospital, and the order of the tasks was kept constant across all children. Cognitive development was examined with the Finnish version of the Wechsler Intelligence scale for Children-IV, WISC-IV (Wechsler, 2010). No control group was used for the WISC-IV tasks because up-to-date Finnish normative data were available. Because the full scale intelligence quotient (FSIQ) contains two WM subtests, cognitive development was examined with the GAI derived from the six subtests from the WISC-IV. The GAI, as Wechsler (2003) described, is the sum of the scaled scores for three verbal comprehension subtests and three perceptual reasoning subtests. Delayed cognitive development was defined as a GAI below 85/– 1.0 *SD*.

WM domains were assessed using two tests for each domain of Baddeley's working memory model. Two subtests (digit recall backwards and digit recall) were from the WISC-IV, and four subtests (counting recall, block recall, maze recall, and nonword recall—Finnish version) were from the WMTB-C (Pickering & Gathercole, 2001). Regarding the subtests from the WMTB-C, the Finnish sample data were collected as described earlier. The Finnish translation and the original test design were applied, and the original British norms were used for comparisons.

All of the standard Z-scores of the six WM subtests were scaled to equal a mean score of 100 and a standard deviation of 15. Each WM domain consisted of two WM subtests. The mean of these two subtests was taken as a measure that represented the child's performance in the particular WM domain. Impaired WM was defined as a score ≤ 77.5/– 1.5 *SD*.

Central executive. The CE domain was assessed with the digit recall backward subtest from the WISC-IV and with the counting recall subtest from the WMTB-C. The digit recall backward subtest is a subtest wherein a child has to recall a sequence of spoken digits in reverse order. The digits are presented one second apart. Lists are constructed randomly and without replacement by digits between one and nine. Two practice trials are given. The length of the list is increased by one digit if two lists of the same length are repeated correctly. In the counting recall test, the child has to simultaneously process and maintain information in WM by counting aloud arrays of dots presented on a series of cards and recalling the tallies in the order the arrays were presented. Six trials form a block, and all trials in a particular block are of the same difficulty level. For each new block, the number of items is increased by one.

Visuospatial sketchpad. VS was measured by block recall and maze recall subtests from the WMTB-C. In the block recall subtest, the examiner taps sequences using the randomly arranged blocks on the block board at the rate of one block per second. The child tries to recall each sequence in the correct order starting from tapping one block. Every trial sequence has six trials, and for each new sequence, the number of taps is increased by one. The maze recall subtest includes two-dimensional mazes and routes. The route is marked on the mazes in red but is also traced with the examiner's finger. After demonstrating the route, the child has to recall it by drawing it in a booklet. The mazes increase in size by one wall and become more complex after each completed trial block.

Phonological loop. PL was assessed with the digit recall subtest from the WISC-IV and with the Finnish version of the nonword recall subtest from the WMTB-C. In the digit recall subtest, the examiner presents sequences of digits at the rate of one per second, and the child tries to recall these sequences in the correct order. Similar to the digit recall backward subtest, the digit lists are constructed randomly and without replacement by digits between one and nine in increasing length. The nonword recall subtest (Finnish version) involves the spoken presentation of sequences of words with two syllables for immediate recall. The stimuli are nonsense words that have been created using common Finnish syllables. The subtest starts with one nonword, and after passing the block of six trials, the number of nonwords increases by one.

The Brain Magnetic Resonance Imaging of VLBW Children

Brain MRI was performed at term age without anesthesia or pharmacological sedation during the infant's postprandial sleep. Ninety-four children of the 95 VLBW children were successfully scanned. The mean age at scanning was 0.1 days after term-equivalent age (*SD* =

2.7 days, range of six days before term-equivalent age to 10 days after term-equivalent age). Ear protection was used during imaging (3M Disposable Ear Plugs 1100, 3M, Brazil and Würth Hearing Protector Art-Nr. 899 300 232, Würth, Austria). The MRI equipment was an open 0.23 Tesla Outlook GP (Philips Medical Inc., Vantaa, Finland).

One experienced neuroradiologist (R. P.) analyzed and categorized MRI images according to the modified scoring system of Maalouf et al. (1999, 2001). The classification of the width of the extracerebral space was completed according to McArdle et al. (1987). MRI findings were categorized into three groups: 1) normal (normal brain anatomy, width of extracerebral space ≤ 4 mm), 2) minor brain abnormality (intraventricular hemorrhages, IVH, grades 1 to 2, caudothalamic cysts, an extracerebral space width of 5 mm), or 3) major brain abnormality (IVH grades 3–4, hemorrhage of the brain parenchyma, white matter cysts, abnormal T1 or T2 signals in the cortex, basal ganglia, thalamus, the cerebellum or internal capsule, abnormality of the corpus callosum, an extracerebral space width of 6 mm or more, and ventriculitis). The neuroradiologist was blinded to the clinical information.

Statistical Analysis

Statistical analyses were performed using SAS version 9.3. Background characteristics were compared between participants and nonparticipants using a chi-squared test for nominal variables, a chi-squared test for trend for ordinal variables, and independent sample *t*-tests for continuous variables. When comparing the WM performance of VLBW children to normative data and to the performance of the Finnish sample group, one sample *t*-test was used. To investigate the possible differences in the mean values of the WM domains among the brain pathology groups (normal, minor, major), a one-way analysis of variance was used. To investigate the correlational structure of the WM of VLBW children, the associations among continuous variables (CE, VS, PL) were studied using Pearson’s correlation coefficient.

Results

The WM Performance of VLBW Children

In the VLBW group, the mean age at the assessment for this study was 11.19 years (*SD* = 0.26, range 10.75–11.66 years). In the sample group for the four WMTB-C subtests, the mean age was 11.32 years (*SD* = 0.28, range 10.79–11.89 years). Of all 95 VLBW children, delayed cognitive development (GAI < 85) was found in 27 (28%). The WM performance of VLBW children in all three WM domains and subtests compared to the test norms is shown in Table 2. VLBW children performed significantly more poorly compared to test norms in the domains of CE and VS. The difference persisted when VLBW children with delayed cognitive development (GAI < 85) were excluded. On the contrary, in the PL domain, the performance of VLBW children was above the norm, and impaired PL was rare. The WM performance of the Finnish sample group in four subtests derived from WMTB-C and in the VS is shown in the Appendix.

(Table 2 about here)

The WM Performance in Relation to the Degree of Brain Pathology

VLBW children were categorized into three brain pathology groups as described earlier. The WM performance of these children according to the findings in the MRI is shown in Table 4. No statistically significant difference was found between these groups in the CE domain (normal vs. minor: $p = .88$, normal vs. major: $p = .13$, and minor vs. major: $p = .48$). Compared to the test norms, all three groups performed significantly more poorly.

With respect to the VS, children with major pathology performed significantly more poorly than did children with normal or minor findings (normal vs. major: $p = .001$ and minor vs. major: $p = .01$). No significant difference was found between groups with normal and minor findings ($p = 1.00$). However, all VLBW groups had weaker VS capacity compared to the test norms.

With respect to the PL functions, the performance of children with major pathology was significantly poorer than that of children with normal findings (normal vs. major: p = .02). No significant difference was found between groups with normal and minor findings (p = 1.0). It is notable that the PL performance of VLBW children with normal findings or minor pathology was above the test norms. The results of the major pathology group did not differ significantly from the test norms.

(Table 3 about here)

Correlations among the WM Domains of VLBW Children

The correlations among the WM domains of the VLBW children differed from earlier studies using Baddeley's tripartite model. When all of the VLBW children (n = 95) were included in the analysis, moderate correlations with statistical significance were found among all three WM domains (CE and VS: r = .40, p < .001; CE and PL: r = .39, p < .001; VS and PL: r = .34, p < .001). When only children with GAI ≥ 85 were included (n = 68), the correlations followed Baddeley's model with statistical significance but with moderate to low correlations between the CE and the VS and also between the CE and the PL (see Figure 1.). As in the original model, no significant correlation was found between the VS and the PL.

(Figure 1 about here)

Discussion

To our knowledge, this is the first study with a comprehensive and theory-based analysis according to Baddeley's model (Baddeley & Hitch, 1974) on the WM performance of VLBW children and on the correlations between WM domains. The VLBW children in this study differed from normative populations in performance and in the correlational structure of the WM, regardless of their levels of cognitive development or the severity of their brain pathology. The overall WM performance of VLBW children at the age of 11 years was significantly poorer than that of the normative population, although recently, some studies have reported more encouraging results with respect to very preterm children's cognitive outcomes (Lind et al., 2011; Luu, Vohr, Allan, Schneider, & Ment, 2011; Munck et al., 2010).

When analyzing the performance of VLBW children in different WM domains, clear deficits of CE functions were found. Despite normal cognitive development (GAI ≥ 85), CE impairment rate was relatively high (38%). When considering the role of CE in attention controlling as Baddeley (1996) described, the results here are not surprising, as a strong connection between prematurity and attention deficits has been shown (e.g., Sucksdorff et al., 2015). Earlier studies using memory tasks similar to those in this study have also shown impairments in the CE memory functions of VLBW children (Aarnoudse-Moens et al., 2012; Clark & Woodward, 2010). According to the recent review by Nosarti and Froudist-Walsh (2016), altered hippocampal-cortical networks especially may be the cause of low CE domain performance along with the white matter abnormalities that Clark and Woodward (2010) showed earlier.

Moreover, the deficits in the VS domain found in the VLBW group were highly expected due to strong evidence from earlier studies (e.g., de Kieviet et al., 2012; Jongbloed-Pereboom et al., 2012). Poor VS performance may result from the deficits in visuospatial and sensorimotor processing abilities, which have been found in preterm children without any cognitive impairment (Kallankari, Kaukola, Olsén, Ojaniemi, & Hallman, 2015). Behind these deficits may also be remarkable altered cortical network dynamics as Doesburg et al. (2011) showed earlier. Moiseev, Doesburg, Herdman, Ribary, and Grunau (2015) identified disturbed activation especially in the middle frontal gyrus, middle temporal gyrus, and post-central gyrus during preterm children's VS performance. Considering this, the incidence of VS impairment was moderately low (18%) in this particular VLBW group.

Studies on PL and other verbal memory functions of VLBW children have been heterogeneous with respect to the definitions and tests used (e.g., Dall'Oglio et al., 2010; Luu et al., 2011) or not (e.g., Fraello et al., 2011; Lind et al., 2011). Consequently, the results are difficult to compare. In line with findings in the present study, Fraello et al. (2011) showed that the PL functions remained mainly intact in the VLBW group. It is of interest that this regional cohort of Finnish VLBW children performed better compared to British normative data. Only 2% of these VLBW children had impaired PL functions. The applied method was similar to the original British one, but linguistic dissimilarities may partly explain the higher scores in Finnish children. Thompson et al. (2014) and Omizzolo et al. (2013) also noticed this tendency of relative fluent performance in memory tasks concerning the PL domain. The suggestion is that, despite preterm birth, brain areas processing phonological information (e.g., activation of the inferior parietal gyrus and inferior and middle frontal gyri) are usually spared (Logie et al., 2003). Clark and Woodward (2010) also suggested that the white matter tracts in the left hemisphere that are specialized for verbal functions remain more intact compared to the right hemisphere. It is noteworthy that VLBW children succeeded well with the simpler verbal memory tasks of PL, whereas clear deficits were seen in the more demanding verbal memory tasks of CE. This is in line with a recent study by Wehrle et al. (2016), who proposed that the determinant seems to be the increasing complexity of the tasks and, accordingly, the increasing demand on the executive functions.

In this study, even VLBW children with normal brain imaging findings showed deficits in the WM performance of the CE domain. No statistically significant difference was found between brain pathology groups in the CE domain, although a difference between the mean scores in normal versus major groups was 10.38 points, having clinical significance. Impairments in VS functions were also obvious in all brain MRI groups, but they were significantly distinct in the VLBW group with major brain pathology. This group of children also performed more poorly but still within the normal range in PL tasks, having more than a10-point-lower mean score compared to the groups with normal brain imaging findings or minor brain pathology.

In earlier studies of preterm-born children, Omizzolo et al. (2014) found a significant association between WM and abnormalities of the basal ganglia, and Zubiaurre-Elorza et al. (2012) found such between WM and the periventricular leukomalacia together with thalamic reductions. Additionally, contradictory findings regarding the connection between memory and the alterations of the regional white matter microstructure have been reported (e.g., Counsell, 2008; Thompson et al., 2014). Furthermore, in their recent study, Moiseev et al. (2015) concluded that the reduced frontal gamma-band activation of preterm children may especially lead to a decreased ability to provoke the interaction between the frontal and other brain areas needed in WM performance.

When considering the correlations between WM domains in the whole VLBW group, the correlation structure of Baddeley's model does not apply. In the present study, the subgroup of VLBW children (GAI $\geq$ 85) showed low to moderate correlations between CE and PL, and CE and VS, while previous studies in normative populations have shown very high correlations (Gathercole et al., 2004; Michalczyk et al., 2013). In addition, PL and VS domains in this study were not as distinct from each other as in normative populations as Gathercole et al. (2004) and Michalczyk et al. (2013) described. Earlier, altered WM structure had been found to be in another specific group of children and adolescents with minor to major cognitive impairments (van der Molen, 2010). To our knowledge, no previous studies on the WM structure of VLBW children exist. However, due to different analysis methods, it is not possible to show the causative factor (e.g., VLBW children) for the discrepancies in the correlations.

The strengths of this study are a well-defined regional VLBW cohort with a long follow-up period. We could also take advantage of the brain MRI administered to all VLBW children at term age. In addition, we were able to take into account the level of cognitive development, as it was assessed at the same time as the WM functions. WM was studied with a comprehensive theoretical framework that had not been used before on VLBW children. Also, the age for assessment was clinically relevant, as the functional organization of WM starts to resemble that of adults at the age of 9 to 10 years (Farber & Beteleva, 2011).

The challenge of WM research in a VLBW group is the application of various and partly overlapping concepts, which makes it difficult to compare the results among different studies. This complexity is also manifested in two recent reviews (Jongbloed-Pereboom et al., 2012; Nosarti & Froudist-Walsh, 2016). In these reviews, the authors pointed out the vast diversity in inclusion and exclusion criteria (e.g., gestational age, birth weight, degree of brain pathology), tests used, and methodologies. In some studies, WM has been defined as separate and specific memory tasks; in other studies, it has been defined as a subdomain of CE functions (Miyake et al., 2000) or as a relatively independent hypernym (Baddeley & Hitch, 1974). Moreover, concepts referring to the preterm born are defined in diverse ways, and caution in integrating study findings is needed. A limitation of this study is that WM was studied with tasks from two separate tests and without a control group. However, the test norms of WISC-IV were up to date and the norms for digit recall and backward digit recall subtests were released separately for the purposes of this particular substudy. The sample group was gathered to study whether the subtests of WMTB-C could be applied in Finnish children in this age group. The Finnish translation and the original test design were applicable, and the original British norms were used for comparisons. It is notable that the Finnish sample group had higher scores in the block recall and nonword recall subtests compared to the British norms. Accordingly, the outperformance of the sample of Finnish children compared to the British norms of the WMTB-C underline the true nature of WM problems, especially in VS in VLBW children. Another limitation is that both chosen CE measures target verbal CE. Nonverbal CE was not measured because the WMTB-C protocol used in the present study does not include nonverbal CE measures. The effect of being multiple was not addressed because the focus in this study was to compare the degree of brain pathology and WM performance. However, shared family environment may have an effect on the performance level. Also, the statistical power of the study is limited due to the small sample sizes, especially in minor and major brain pathology groups. Therefore, conclusions from these analysis must be drawn with caution, and one must be aware of a potential type 2 error. In addition, this study is cross-sectional and does not provide information on the maturing processes of WM in VLBW children by time.

Conclusion

This study highlights the importance of assessing the WM functions of VLBW children at school age. VLBW children with significant developmental problems are typically referred to follow-up, but those without severe or wide-ranging problems usually drop out from follow-up when they enter compulsory education. This study shows that even VLBW children with normal cognitive development or normal neonatal MRI findings are at risk for WM deficits, especially in the domains of CE and VS. These children may not exhibit problems in early developmental follow-up because WM develops gradually, and the demand for memory and more complex learning increases with age. Further studies are needed to explore the optimal timing of the assessment of WM functions and interventions to avoid the potential academic underachievement of VLBW children.

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Appendix

Working memory (WM) Performance of the Finnish Sample Group

The Finnish sample group outperformed the British normative data in two subtests, the block recall and the nonword recall (see Table A1). On the other hand it scored under the British mean in the counting recall subtest. When the performance of the VLBW children was compared to this Finnish sample group, their underachievement was obvious in the subtests of the visuospatial sketchpad despite the level of cognitive development ($p < .001$). Also in the counting recall subtest the sample group performed significantly better compared to the whole VLBW group ($p < .001$) or to those with GAI ≥ 85 ($p < .01$). Considering the nonword subtest there was no statistically significant difference when the performance of VLBW children was compared to the Finnish sample group ($p = .65$). This applied also when VLBW children with delayed cognitive development (GAI < 85) were excluded ($p = .07$).

(Table A1 about here)

Table 1 The Neonatal Characteristics and Parental Education of Very Low Birth Weight (VLBW) Children. Data are presented in number and % if not otherwise indicated.

Variable	VLBW (*n* = 95)
Prenatal corticosteroids	91 (96%)
Multiple birth	33 (35%)
Birth weight (g)	
Mean (SD) [min, max]	1047.75 (269.10) [400, 1500]
Gestational age (weeks)	
Mean (SD) [min, max]	28.50 (2.66) [23, 36]
Small for gestational age*	34 (36%)
Male	49 (52%)
Intestinal perforation (NEC included)	4 (4%)
Sepsis or meningitis	24 (25%)
Ductal ligation	13 (14%)
Bronchopulmonary dysplasia (BPD)	15 (16%)
Retinopathy of prematurity ≥ grade III	1 (1%)
Brain MRI grading	
normal	56 (60%)
minor pathology	18 (19%)
major pathology	20 (21%)
Maternal education	
9 years	9 (10%)
> 9 – 12 years	23 (24%)

> 12 years	62 (66%)
Paternal education	
9 years	9 (10%)
> 9 – 12 years	54 (57%)
> 12 years	31 (33%)

* Small for gestational age (SGA) was defined as a birth weight of < - 2.0 *SD* according to age and gender specific Finnish growth charts.

Table 2 Working Memory (WM) Performance of Very Low Birth Weight (VLBW) Children in Each WM Domain and Subtests Including All Children and Separately Those with General Ability Index (GAI) ≥ 85, and Compared to the Test Norms. Data are shown as *n*, mean (*M*), (*SD*), [min, max], *p*. In normative group *M* = 100, (*SD* = 15).

WM DOMAIN **Subtest**	**VLBW (n = 95)**	**VLBW, GAI ≥ 85 (n = 68)**
CENTRAL EXECUTIVE	n = 95, 83.91 (20.56) [55, 132], $p < .001$	n = 68, 87.64 (20.54) [59, 132], $p < .001$
impaired[a] CE, n (%)	n = 46 (48%)	n = 26 (38%)
Counting Recall	n = 95, 85.13 (14.08) [55, 108], $p < .001$	n = 68, 87.49 (12.76) [55, 108], $p < .001$
Backward Digit	n = 95, 82.68 (34.67) [55, 165], $p < .001$	n = 68, 87.79 (36.07) [55, 165], $p < .01$
VISUOSPATIAL SKETCHPAD	n = 94, 89.10 (12.06) [57, 111], $p < .001$	n = 68, 91.65 (11.03) [59, 111], $p < .001$
impaired[a] VS, n (%)	n = 18 (18%)	n = 10 (15%)
Block Recall	n = 95, 87.69 (13.90) [57, 125], $p < .001$	n = 68, 91.24 (12.83) [61, 125], $p < .001$
Mazes Memory	n = 94, 90.18 (16.45) [57, 121], $p < .001$	n = 68, 92.07 (15.84) [57, 121], $p < .001$
PHONOLOGICAL LOOP	n = 95, 107.82 (15.31) [60, 145], $p < .001$[b]	n = 68, 110.79 (13.79) [83, 145], $p < .001$[b]
impaired[a] PL, n (%)	n = 2 (2%)	n = 0 (0%)
Digit Recall	n = 95, 103.74 (15.18) [55, 145], $p = .02$[b]	n = 68, 105.96 (14.44) [75, 145], $p < .01$[b]
Nonword Recall	n = 95, 111.91 (18.47) [59, 145], $p < .001$[b]	n = 68, 115.63 (16.57) [70, 145], $p < .001$[b]

[a] Impairment is defined as ≤ -1.5 *SD* from mean of the test norms.

[b] The difference between VLBW children and the test norms is positive for the VLBW group.

Table 3 Working Memory (WM) Performance of Very Low Birth Weight Children (VLBW) in Each WM Domain and Subtests According to Degree of Brain Pathology Findings in MRI and Compared to the Test Norms. Data are shown as *n*, mean (*M*), (*SD*), [min, max], *p*. In normative group $M = 100$, ($SD = 15$).

WM DOMAIN Subtests	Normal findings ($n = 56$)	Minor findings ($n = 18$)	Major findings ($n = 20$)
CENTRAL EXECUTIVE	$n = 56$, 86.81 (20.46) [55, 130], $p < .001$	$n = 18$, 84.14 (17.00) [64, 120], $p < .001$	$n = 20$, 76.43 (22.82) [55, 132], $p < .001$
impaired[c] CE, *n* (%)	$n = 23$ (41%)	$n = 8$ (44%)	$n = 14$ (70%)
Counting Recall	$n = 56$, 86.48 (13.38) [55, 108], $p < .001$	$n = 18$, 89.94 (8.50) [72, 98], $p < .001$	$n = 20$, 77.85 (17.28) [55, 101], $p < .001$
Backward Digit	$n = 56$, 87.14 (35.20) [55, 165], $p < .01$	$n = 18$, 78.33 (32.76) [55, 145], $p = .012$	$n = 20$, 75.00 (35.28) [55, 165], $p < .01$
VISUOSPATIAL SKETCHPAD	$n = 56$, 91.38 (10.39) [69, 111], $p < .001$	$n = 18$, 91.33 (10.05) [71, 107], $p = .002$	$n = 20$, 80.29 (14.96) [57, 109], $p < .001$
impaired[c] VS, *n* (%)	$n = 6$ (11%)	$n = 3$ (17%)	$n = 9$ (45%)
Block Recall	$n = 56$, 90.64 (12.96) [61, 125], $p < .001$	$n = 18$, 88.78 (11.52) [69, 117], $p = .001$	$n = 20$, 78.00 (14.85) [57, 109], $p < .001$
Mazes Memory	$n = 56$, 92.13 (15.12) [57, 121], $p < .001$	$n = 18$, 93.89 (13.26) [60, 109], $p = .07$	$n = 20$, 81.47 (20.56) [57, 121], $p = .001$
PHONOLOGICAL LOOP	$n = 56$, 109.92 (12.41) [89, 145], $p < .001$[d]	$n = 18$, 109.67 (14.28) [85, 143], $p = .01$[d]	$n = 20$, 99.33 (20.50) [60, 138], $p = .88$
impaired[c] PL, *n* (%)	$n = 0$ (0%)	$n = 0$ (0%)	$n = 2$ (10%)
Digit Recall	$n = 56$, 104.20 (13.20) [75, 145], $p = .02$[d]	$n = 18$, 106.90 (14.77) [95, 140], $p = .06$	$n = 20$, 98.25 (19.01) [55, 140], $p = .69$
Nonword Recall	$n = 56$, 115.60 (14.90) [81, 145], $p < .001$[d]	$n = 18$, 112.40 (17.67) [75, 145], $p < .01$[d]	$n = 20$, 100.40 (24.01) [59, 145], $p = .94$

[c] Impairment is defined as a score ≤ -1.5 *SD* from mean of the test norms.

[d] The difference between VLBW children and the test norms is positive for the VLBW group with normal or minor findings.

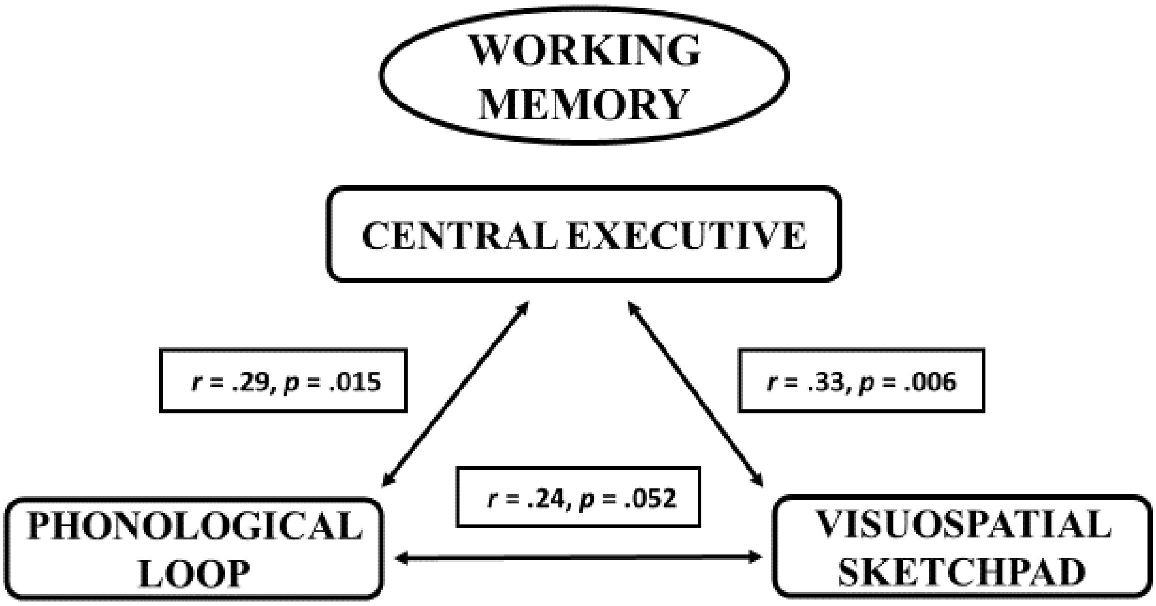

Figure 1 Correlations between Working Memory Domains of Very Low Birth Weight Children with General Ability Index (GAI) ≥ 85.

Appendix

Working memory (WM) Performance of the Finnish Sample Group

The Finnish sample group outperformed the British normative data in two subtests, the block recall and the nonword recall (see Table A1). On the other hand it scored under the British mean in the counting recall subtest. When the performance of the VLBW children was compared to this Finnish sample group, their underachievement was obvious in the subtests of the visuospatial sketchpad despite the level of cognitive development ($p < .001$). Also in the counting recall subtest the sample group performed significantly better compared to the whole VLBW group ($p < .001$) or to those with GAI ≥ 85 ($p < .01$). Considering the nonword subtest there was no statistically significant difference when the performance of VLBW children was compared to the Finnish sample group ($p = .65$). This applied also when VLBW children with delayed cognitive development (GAI < 85) were excluded ($p = .07$).

Table A1 Working Memory (WM) Performance of the Finnish Sample Group in Four WM Subtests Derived from WMTB-C and Compared to the Test Norms. Data are shown as *n*, mean (*M*), (*SD*), [min, max], *p*. In normative data $M = 100$, ($SD = 15$).

WM DOMAIN **Subtests**	**Finnish Sample Group (*n* = 68)**
Counting Recall	$n = 68$, 95.44 (15.56) [59, 144], $p = .02$
VISUOSPATIAL SKETCHPAD	$n = 68$, 105.80 (14.21) [68, 135], $p < .01$[a]
Block Recall	$n = 68$, 108.80 (17.67) [65, 145], $p < .001$[a]
Mazes Memory	$n = 68$, 102.80 (14.79) [66, 132], $p = .12$
Nonword Recall	$n = 68$, 110.70 (14.96) [86, 140], $p < .001$[a]

[a]The difference between the Finnish sample group and the test norms is positive for the sample group.